Amendments to the Specification:

Please replace the paragraph at page 1, lines 4-16, with the following amended paragraph:

This application is a continuation-in-part of U.S. Serial No. 10/399,213, filed April 14, 2003, (abandoned), which is a national phase filing of PCT AU01/01291, filed October 15, 2001, which is a PCT filing of AU provisional application PR0745, filed October 13, 2000. This application is also a continuation-in-part of U.S. Serial No. 60/527001, filed December 5, 2003. This application is also a continuation-in-part of U.S. Serial No. 10/418,747, filed April 18, 2003, (abandoned), which is a continuation-in-part of U.S. Serial No. 09/977,479, filed October 12, 2001, (abandoned), which is a continuation-in-part of U.S. Serial No. 09/965,394 filed September 26, 2001 (abandoned), which is a continuation-in-part of U.S. Serial No. 09/755,965, filed January 5, 2001 (abandoned), which is a continuation-in-part of U.S. Serial No. 09/795,286, filed October 13, 2000, (abandoned), which is a continuation-in-part of AU provisional application PR0745, filed October 13, 2000, and of U.S. Serial No. 09/795,302, filed October 13, 2000 (abandoned), which is a continuation-in-part of PCT AU00/00329, filed April 17, 2000, which is a PCT filing of AU provisional application PP9778 filed April 15, 1999. Each of these applications is hereby incorporated by reference.

Please replace the paragraph at page 35, lines 17-30, with the following amended paragraph:

Administration may be by any method which delivers the sex steroid-ablating agent into the body. Thus, the sex steroid-ablating agent may be administered, in accordance with the invention, by any route including, without limitation, intravenous, subdermal, subcutaneous, intramuscular, topical, and oral routes of administration. One non-limiting example of administration of a sex steroid-ablating agent is a subcutaneous/intradermal injection of a "slow-release" depot of GnRH agonist (*e.g.*, one, three, or four month ~~Lupron®~~ LUPRON® injections) or a subcutaneous/intradermal injection of a "slow-release" GnRH-containing implant (*e.g.*, one or three month ~~Zoladex®~~ ZOLADEX®, *e.g.*, 3.6 mg or 10.8 mg implant). These

could also be given intramuscularly (i.m.), intravenously (i.v.) or orally, depending on the appropriate formulation. Another example is by subcutaneous injection of a "depot" or "impregnated implant" containing, for example, about 30 mg of ~~Lupron®~~ LUPRON® (*e.g.*, ~~Lupron Depot®~~ LUPRON DEPOT®, (leuprolide acetate for depot suspension) TAP Pharmaceutical Products, Inc., Lake Forest, IL). A 30 mg ~~Lupron®~~ LUPRON® injection is sufficient for four months of sex steroid ablation to allow the thymus to rejuvenate and export new naïve T cells into the blood stream.

Please replace the paragraph at page 36, lines 1-25, with the following amended paragraph:

In some embodiments, sex steroid ablation or inhibition of sex steroid-signaling is accomplished by administering an anti-androgen such as an androgen blocker (*e.g.*, bicalutamide, trade names ~~Cosudex® or Casodex®~~ COSUDEX® or CASODEX®, AstraZeneca, Auckland, NZ), either alone or in combination with an LHRH analog or any other method of castration. Sex steroid ablation or interruption of sex steroid-signaling may also be accomplished by administering cyproterone acetate (trade name, ~~Androcur®~~ ANDROCOR®, Schering AG, Germany; *e.g.*, 10-1000 mg, 100 mg bd or tds, or 300 mg IM weekly, a 17-hydroxyprogesterone acetate, which acts as a progestin, either alone or in combination with an LHRH analog or any other method of castration. Alternatively, other anti-androgens may be used (*e.g.*, antifungal agents of the imidazole class, such as liarozole (~~Liazol®~~ LIAZOL®, *e.g.*, 150 mg/day, an aromatase inhibitor) and ketoconazole, bicalutamide (trade name ~~Cosudex® or Casodex®~~ COSUDEX® or CASODEX®, 5-500 mg, *e.g.*, 50 mg po QID), flutamide (trade names ~~Euflex® and Eulexin®,~~ EUFLEX® and EULEXIN®, Schering Plough Corp, N.J.; 50-500 mg *e.g.*, 250 or 750 po QID), megestrol acetate (~~Megace®~~ MEGACE®) *e.g.*, 480-840 mg/day or nilutamide (trade names ~~Anandron®, and Nilandron®,~~ ANANDRON®, and NILANDRON®, Roussel, France *e.g.*, orally, 150-300 mg/day)). Antiandrogens are often important in therapy, since they are commonly utilized to address flare by GnRH analogs. Some antiandrogens act by inhibiting androgen receptor translocation, which interrupts negative feedback resulting in increased testosterone levels and minimal loss of libido/potency. Another class of anti-androgens useful

in the present invention are the selective androgen receptor modulators (SARMS) (*e.g.*, quinoline derivatives, bicalutamide (trade name ~~Cosudex® or Casodex®~~ COSUDEX® or CASODEX®, ICI Pharmaceuticals, England *e.g.*, orally, 50 mg/day), and flutamide (trade name ~~Eulexin®,~~ EULEXIN®, *e.g.*, orally, 250 mg/day)). Other well known anti-androgens include 5 alpha reductase inhibitors (*e.g.*, dutasteride, (*e.g.*, 0.5 mg/day) which inhibits both 5 alpha reductase isoenzymes and results in greater and more rapid DHT suppression; finasteride (trade name ~~Proscar®;~~ PROSCAR®; 0.5-500 mg, *e.g.*, 5 mg po daily), which inhibits 5 alpha reductase 2 and consequent DHT production, but has little or no effect on testosterone or LH levels).

Please replace the paragraph bridging pages 36 and 37, with the following amended paragraph:

In other embodiments, sex steroid ablation or inhibition of sex steroid-signaling is accomplished by administering anti-estrogens either alone or in combination with an LHRH analog or any other method of castration. Some anti-estrogens (*e.g.*, anastrozole (trade name ~~Arimidex®~~ ARIMIDEX®), and fulvestrant (trade name ~~Faslodex®~~ FASLODEX®) act by binding the estrogen receptor (ER) with high affinity similar to estradiol and consequently inhibiting estrogen from binding. ~~Faslodex®~~ FASLODEX® binding also triggers conformational change to the receptor and down-regulation of estrogen receptors, without significant change in FSH or LH levels. Other non-limiting examples of anti-estrogens are tamoxifen (trade name ~~Nolvadex®~~ NOLVADEX®); Clomiphene (trade name ~~Clomid®~~ CLOMID®) *e.g.*, 50-250 mg/day, a non-steroidal ER ligand with mixed agonist/antagonist properties, which stimulates release of gonadotrophins; Fulvestrant (trade name ~~Faslodex®~~ FASLODEX® 10-1000 mg, *e.g.*, 250 mg IM monthly); diethylstilbestrol ((DES), trade name ~~Stilphostrol®~~ STILPHOSTROL®) *e.g.*, 1-3 mg/day, which shows estrogenic activity similar to, but greater than, that of estrone, and is therefore considered an estrogen agonist, but binds both androgen and estrogen receptors to induce feedback inhibition on FSH and LH production by the pituitary, diethylstilbestrol diphosphate *e.g.*, 50 to 200 mg/day; as well as danazol, droloxifene, and iodoxyfene, which each

act as antagonists. Another class of anti-estrogens which may be used either alone or in combination with other methods of castration, are the selective estrogen receptor modulators (SERMS) (*e.g.*, toremifene (trade name ~~Fareston®,~~ FARESTON®, 5-1000 mg, *e.g.*, 60 mg po QID), raloxofene (trade name ~~Evista®~~ EVISTA®), and tamoxifen (trade name ~~Nolvadex®,~~ NOLVADEX®, 1-1000 mg, *e.g.*, 20 mg po bd), which behaves as an agonist at estrogen receptors in bone and the cardiovascular system, and as an antagonist at estrogen receptors in the mammary gland). Estrogen receptor downregulators (ERDs) (*e.g.*, tamoxifen (trade name, ~~Nolvadex®,~~ NOLVADEX®)) may also be used in the present invention.

Please replace the paragraph bridging pages 37 and 38, with the following amended paragraph:

Other non-limiting examples of methods of inhibiting sex steroid-signaling which may be used either alone or in combination with other methods of castration, include aromatase inhibitors and other adrenal gland blockers (*e.g.*, Aminoglutethimide, formestane, vorazole, exemestane, anastrozole (trade name ~~Arimidex®,~~ ARIMIDEX®, 0.1-100 mg, *e.g.*, 1 mg po QID), which lowers estradiol and increases LH and testosterone), letrozole (trade name ~~Femara®,~~ FEMARA®, 0.2-500 mg, *e.g.*, 2.5 mg po QID), and (trade name ~~Aromasin®~~ AROMASIN®) 1-2000 mg, *e.g.*, 25 mg/day); aldosterone antagonists (*e.g.*, spironolactone (trade name, ~~Aldactone®~~ ALDACTONE®) *e.g.*, 100 to 400 mg/day), which blocks the androgen cytochrome P-450 receptor;) and eplerenone, a selective aldosterone-receptor antagonist) antiprogestogens (*e.g.*, medroxypregesterone acetate, *e.g.*, 5 mg/day, which inhibits testosterone syntheses and LH synthesis); and progestins and anti-progestins such as the selective progesterone response modulators (SPRM) (*e.g.*, megestrol acetate *e.g.*, 160 mg/day, mifepristone (RU 486, ~~Mifeprex®,~~ MIFEPREX®, *e.g.*, 200 mg/day); and other compounds with estrogen/antiestrogenic activity, (*e.g.*, phytoestrogens, flavones, isoflavones and coumestan derivatives, lignans, and industrial compounds with phenolic ring (*e.g.*, DDT)). Also, anti-GnRH vaccines (see, *e.g.*, Hsu *et al.*, (2000) *Cancer Res.* 60:3701; Talwar, (1999) *Immunol. Rev.* 171:173-92), or any other pharmaceutical which mimics the effects produced by the aforementioned drugs, may also be used. In

addition, steroid receptor based modulators, which may be targeted to be thymic specific, may also be developed and used. Many of these mechanisms of inhibiting sex steroid-signaling are well known. Each drug may also be used in modified form, such as acetates, citrates and other salts thereof, which are well known to those in the art.

Please replace the paragraph bridging pages 38 and 39, with the following amended paragraph:

In some embodiments, the sex steroid-mediated signaling to the thymus is disrupted by administration of a sex steroid analog, such as an analog of leutinizing hormone-releasing hormone (LHRH). Sex steroid analogs are commercially known and their use in therapies and chemical castration are well known. Such analogs include, but are not limited to, the following agonists of the LHRH receptor (LHRH-R): buserelin (*e.g.*, buserelin acetate, trade names ~~Suprefact®~~ SUPREFACT® (*e.g.*, 0.5-02 mg s.c./day), ~~Suprefact Depot®,~~ SUPREFACT DEPOT®, and ~~Suprefact®~~ SUPREFACT® Nasal Spray (*e.g.*, 2 μg per nostril, every 8 hrs.), Hoechst, also described in U.S. Patent Nos. 4,003,884, 4,118,483, and 4,275,001); ~~Cystorelin®~~ CYSTORELIN® (*e.g.*, gonadorelin diacetate tetrahydrate, Hoechst); deslorelin (*e.g.*, deslorelin acetate, ~~Deslorell®,~~ DESLORELL®, Balance Pharmaceuticals); gonadorelin (*e.g.*, gonadorelin hydrocholoride, trade name ~~Factrel®~~ FACTREL® (100 μg i.v. or s.c.), Ayerst Laboratories); goserelin (goserelin acetate, trade name ~~Zoladex®,~~ ZOLADEX®, AstraZeneca, Auckland, NZ, also described in U.S. Patent Nos. 4,100,274 and 4,128,638; GB 9112859 and GB 9112825); histrelin (*e.g.*, histrelin acetate, ~~Supprelin®,~~ SUPPRELIN®, (s.c., 10 μg/kg/day), Ortho, also described in EP 217659); leuprolide (leuprolide acetate, trade name ~~Lupron® or Lupron Depot®;~~ LUPRON® or LUPRON DEPOT®; Abbott/TAP, Lake Forest, IL, also described in U.S. Patent Nos. 4,490,291 3,972,859, 4,008,209, 4,992,421, and 4,005,063; DE 2509783); leuprorelin (*e.g.*, leuprorelin acetate, trade name ~~Prostap SR®~~ PROSTAP SR® (*e.g.*, single 3.75 mg dose s.c. or i.m./month), ~~Prostap3®~~ PROSTAP3® (*e.g.*, single 11.25 mg dose s.c. every 3 months), Wyeth, USA, also described in Plosker *et al.*, (1994) Drugs 48:930); lutrelin (Wyeth, USA, also described in U.S. Patent No. 4,089,946); ~~Meterelin®~~ METERELIN® (*e.g.*, Avorelina (*e.g.*, 10-15 mg slow-release formulation),

also described in WO 91/18016); nafarelin (*e.g.*, trade name ~~Synarel®~~ SYNAREL® (i.n. 200-1800 μg/day), Syntex, also described in U.S. Patent No. 4,234,571; WO 93/15722; and EP0052510); and triptorelin (*e.g.*, triptorelin pamoate; trade names ~~Trelstar LA®~~ TRELSTAR LA® (11.25 mg over 3 months), ~~Trelstar LA Debioclip®~~ TRELSTAR LA DEBIOCLIP® (pre-filled, single dose delivery), ~~LA Trelstar Depot®~~ LA TRELSTAR DEPOT® (3.75 mg over one month), and ~~Decapeptyl®,~~ DECAPEPTYL®, Debiopharm S.A., Switzerland, also described in U.S. Patent Nos. 4,010,125, 4,018,726, 4,024,121, and 5,258,492; EP 364819). LHRH analogs also include, but are not limited to, the following antagonists of the LHRH-R: abarelix (trade name ~~Plenaxis™~~ PLENAXIS™ (*e.g.*, 100 mg i.m. on days 1, 15 and 29, then every 4 weeks thereafter), Praecis Pharmaceuticals, Inc., Cambridge, MA) and cetrorelix (*e.g.*, cetrorelix acetate, trade name ~~Cetrotide™~~ CETROTIDE™ (*e.g.*, 0.25 or 3 mg s.c.), Zentaris, Frankfurt, Germany). Additional sex steroid analogs include ~~Eulexin®~~ EULEXIN® (*e.g.*, flutamide (*e.g.*, 2 capsules 2x/day, total 750 mg/day), Schering-Plough Corp., also described in FR 7923545, WO 86/01105 and PT 100899), and dioxane derivatives and other LHRH analogs such as are described in EP 181236, U.S. Patent Nos. 4,608,251, 4,656,247, 4,642,332, 4,010,149, 3,992,365, and 4,010,149. Combinations of agonists, combinations of antagonists, and combinations of agonists and antagonists are also included. One non-limiting analog of the invention is deslorelin (described in U.S. Patent No. 4,218,439). For a more extensive list of analogs, see Vickery *et al.* (1984) LHRH and Its Analogs: Contraceptive & Therapeutic Applications (Vickery *et al.*, eds.) MTP Press Ltd., Lancaster, PA. Each analog may also be used in modified form, such as acetates, citrates and other salts thereof, which are well known to those in the art.